

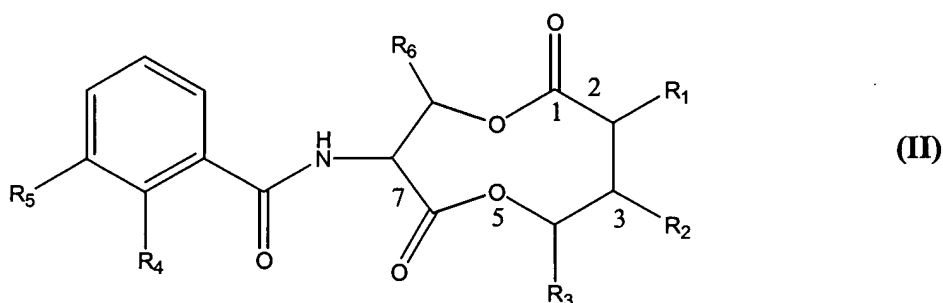
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1.-10. (Canceled)

11. (Currently amended) An apoptotic agent composition that ~~modulates~~ induces apoptosis by binding to a Bcl-2 family member protein and preferentially inducing apoptosis in a cell that over-expresses the Bcl-2 family member protein, the agent composition having the following formula II,



having an absolute configuration of [2R, 3R, 4S, 7S, 8R], and ~~comprising at least a first and a second chemical modification, the first chemical modification decreasing the affinity of the agent for cytochrome B, wherein the first chemical modification is selected from the following:~~

~~R₄ is hydrogen, a C₁-C₈ linear or branched alkane, a C₁-C₈ hydroxyalkane, or a substituted alkyl group; and~~

~~R₅ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₃-C₈ di- or tri-alkylamine, a C₁-C₈ carboxylic acid, a C₂-C₈ amide, or a substituted alkyl group;~~

~~and the second chemical modification is selected from the following: wherein~~

~~R₁ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₁-C₈ di- or tri-amine, a C₁-C₈ amide, a C₁-C₈ carboxylic acid, or a substituted alkyl group;~~

R₂ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₁-C₈ di- or tri-amine, a C₁-C₈ amide, a C₁-C₈ carboxylic acid, or a substituted alkyl group;

R₃ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₁-C₈ di- or tri-amine, a C₁-C₈ amide, a C₁-C₈ carboxylic acid, or a substituted alkyl group; ~~and~~

R₄ is hydrogen, a C₁-C₈ linear or branched alkane, a C₁-C₈ hydroxyalkane, or a substituted alkyl group;

R₅ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₃-C₈ di- or tri-alkylamine, a C₁-C₈ carboxylic acid, a C₂-C₈ amide, or a substituted alkyl group; and

R₆ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₁-C₈ di- or tri-amine, a C₁-C₈ amide, a C₁-C₈ carboxylic acid, or a substituted alkyl group.

12. (Currently amended) The ~~agent~~ composition of claim 11, further comprising a pharmaceutically acceptable carrier.

13. (Currently amended) The ~~agent~~ composition of claim 11 for use in treating an apoptosis-associated disease in a subject in need thereof.

14. (Canceled)

15. (Currently amended) A method for identifying ~~an agent~~ a composition which ~~modulates~~ induces apoptosis of a cell ~~by binding wherein the composition binds~~ to the hydrophobic pocket of ~~an anti-apoptotic Bcl-x_L or Bcl-2 family member protein~~ formed by the BH1, BH2 and BH3 domains of the protein, comprising:

a) admixing a candidate compound with a cell which over-expresses ~~the anti-apoptotic Bcl-x_L or Bcl-2 family member protein~~;

b) admixing the candidate compound with a control cell which does not over-express ~~the anti-apoptotic Bcl-x_L or Bcl-2 family member protein~~; and

c) determining whether the candidate compound ~~modulates~~ induces the activity of ~~the anti-apoptotic Bcl-x_L or Bcl-2 family member protein~~ to produce a physiological change in the cell which over-expresses ~~the anti-apoptotic Bcl-x_L or Bcl-2 family member protein~~ indicative of apoptosis, but does not produce a substantial physiological change in the cell which does not over-express ~~the anti-apoptotic Bcl-x_L or Bcl-2 family member protein~~.

16. (Canceled)

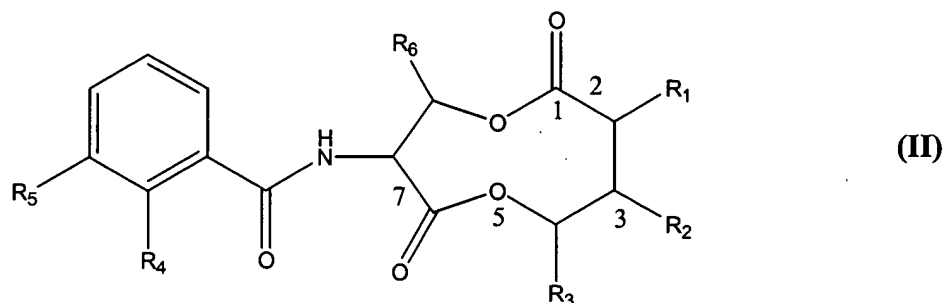
17. (Original) The method of claim 15, wherein the physiological change indicative of apoptosis is cell shrinkage, chromosome condensation and migration, mitochondrial swelling, or disruption of mitochondrial transmembrane potential.

18. (Original) The method of claim 17, wherein the cellular change comprises disruption of mitochondrial transmembrane potential.

19. (Currently amended) The method of claim 15, wherein the cell that over-expresses ~~the anti-apoptotic Bcl-x_L or Bcl-2 family member protein~~ is transfected with a gene which encodes ~~the anti-apoptotic Bcl-x_L or Bcl-2 protein~~.

20. (Canceled)

21. (Currently amended) The A method of claim 20 for treating a subject having an apoptosis-associated disease, comprising administering to the subject a therapeutically effective amount of a wherein the antimycin or antimycin derivative is of the following formula, and having an absolute configuration of [2R, 3R, 4S, 7S, 8R]:



wherein R₁ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₁-C₈ di- or tri-amine, a C₁-C₈ amide, a C₁-C₈ carboxylic acid, or a substituted alkyl group;

R₂ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₁-C₈ di- or tri-amine, a C₁-C₈ amide, a C₁-C₈ carboxylic acid, or a substituted alkyl group;

R₃ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₁-C₈ di- or tri-amine, a C₁-C₈ amide, a C₁-C₈ carboxylic acid, or a substituted alkyl group;

R₄ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ carboxylic acid, or a substituted alkyl group;

R₅ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₁-C₈ di- or tri-alkylamine, a C₁-C₈ amide, a C₁-C₈ carboxylic acid, or a substituted alkyl group; and

R₆ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₁-C₈ di- or tri-amine, a C₁-C₈ amide, a C₁-C₈ carboxylic acid, or a substituted alkyl group.

22. (Original) The method of claim 21, wherein the antimycin derivative is 2-methoxy ether antimycin A or A₃.

23. (Canceled)

24. (Currently amended) The method of claim ~~20~~ 21, wherein the subject is human.

25. (Currently amended) The method of claim ~~20~~ 21, further comprising administering a pharmaceutical carrier.

26. (Currently amended) The method of claim ~~20~~ 21, wherein the administration is intravenous, subcutaneous, intramuscular, intradermal, transdermal, intrathecal, intracerebral, intraperitoneal, epidural or oral.